DETAILED ACTION

Reasons for Allowance

1. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Mr. Shawn Foley (Reg. No. 33,071) on December 3, 2010.

2. The application has been amended as follows:

In the specification:

Replace the first paragraph of page 1 with --- This application claims the priority of US provisional application 60/463,712, filed on April 18, 2003. The invention relates to the novel application of analyte-specific binding components and nucleic acid amplification to provide an ultra-sensitive, high-throughput assay to detect and quantify an analyte in solution ---.

In the claims:

Combining claims 9 and 16-19 with claims 1-8, 10-14, 20, 21, 24-27, 29, 30, 74, and 78.

1. (Currently Amended) A method of detecting an analyte in a sample, comprising:

(i) combining:

(a) an analyte;

(b) a first proximity member, comprising a first analyte-specific binding entity and a [first] single stranded first oligonucleotide comprising a first portion wherein the

first analyte-specific binding entity is capable of forming a complex with the analyte and is conjugated to the first oligonucleotide;

(c) a second proximity member, comprising a second analyte-specific binding entity and a [second] single stranded second oligonucleotide comprising a portion that is capable of hybridizing to the first portion of the first oligonucleotide wherein the second analyte-specific binding entity is capable of forming a complex with the analyte and is conjugated to the second oligonucleotide [oligionucleotide comprising a portion that is capable of hybridizing to the first portion of the first oligonucleotide]; and

(d) a hybridization blocker oligonucleotide at a concentration in excess of the concentrations of the first and second proximity members, wherein the hybridization blocker oligonucleotide comprises a portion that is capable of forming a hybrid with the first portion of the first oligonucleotide to reduce hybridization between the first and second oligonucleotides and wherein the first analyte specific binding entity and/or the second analyte specific binding entity is a protein or a protein complex;

(ii) forming a complex comprising the analyte, the first proximity member, [and] the second proximity member, and the hybridization blocker oligonucleotide that is hybridized with the first portion of the first oligonucleotide;

(iii) forming a hybrid by displacing the hybridization blocker oligonucleotide from the first portion of the first oligonucleotide of the complex wherein the hybrid comprises the first portion of the first oligonucleotide and the portion of the second oligonucleotide, such that [upon hybridization] the 3' terminus of the first oligonucleotide and/ or second

oligonucleotide of the hybrid can [may] be extended via a polymerase;

(iv) extending via a polymerase the 3' terminus of the first oligonucleotide and/ or second oligonucleotide and producing an amplicon;

(v) amplifying the amplicon and producing an amplification product; and

(vi) detecting the amplification product, wherein the detection of the amplification product indicates the presence of the analyte in the sample.

6. (Currently Amended) The method of claim 1, wherein the hybridization blocker oligonucleotide forms a hybrid with the first portion of the first oligonucleotide in the complex and [wherein] the hybridization blocker oligonucleotide contains bases that are complementary with all of the bases of the first portion of the first oligonucleotide.

9. (Currently Amended) The method of claim 1, wherein the hybridization blocker oligonucleotide forms a hybrid with the first portion of the first oligonucleotide in the complex and [wherein the bases of the hybridization blocker oligonucleotide of the hybrid are] less than all of the bases of the first portion of the first oligonucleotide hybridize with the hybridization blocker oligonucleotide in the complex.

10. (Currently Amended) The method of claim 1, further [combining] comprising adding a deblocker oligonucleotide that is capable of reducing the hybridization between the hybridization blocker oligonucleotide and the first oligonucleotide.

16. (Currently Amended) The method of claim 10, wherein the hybridization blocker oligonucleotide [hybridizes with] is displaced from the first portion of the first oligonucleotide in the complex after the addition of the deblocker oligonucleotide.

20. (Currently Amended) The method of claim 1, further comprising adding in step (i) [a second] another hybridization blocker oligonucleotide at a concentration in excess of the concentration of the first and second proximity members, wherein the [second] another hybridization blocker oligonucleotide is capable of hybridizing to the portion of the second oligonucleotide that is capable of forming a hybrid with the first portion of the first oligonucleotide, and wherein said forming a complex in step (ii) further comprises hybridization between the [second] another hybridization blocker oligonucleotide and the portion of the second oligonucleotide, and wherein said forming a hybrid in step [(ii)] (iii) further comprises displacing the second hybridization blocker oligonucleotide.

29. (Currently Amended) The method of claim [28] 1, wherein the protein complex comprises a first protein that is conjugated to the first or second oligonucleotide and a second protein that is capable of forming a complex with the analyte.

74. (Currently Amended) A method of detecting an analyte in a sample, comprising:

(i) combining:

(a) an analyte;

(b) a first proximity member, comprising a first analyte-specific binding entity and a [first] single stranded first oligonucleotide comprising, from 3' to 5', a first portion and a second portion wherein the first analyte-specific binding entity is capable of forming a complex with the analyte and is conjugated to the first oligonucleotide;

(c) a second proximity member, comprising a second analyte-specific binding entity and a [second] single stranded second oligonucleotide comprising, from 5' to 3', a first portion and a second portion, wherein the second analyte-specific binding

entity is capable of forming a complex with the analyte and is conjugated to the second oligonucleotide, wherein the [second] first portion of the first oligonucleotide is capable of hybridizing to the [first] second portion of the second oligonucleotide and the first analyte-specific binding entity and/or second analyte-specific binding entity is/are a protein or proteins which is/are capable of directly binding to the analyte;

(ii) forming a complex comprising the analyte, the first proximity member, and the second proximity member, wherein the complex contains a hybrid comprising the [second] first portion of the first oligonucleotide and the second portion of the second oligonucleotide[,wherein upon hybridization] such that only the 3' terminus of the second portion of the second oligonucleotide [is the on 3' terminus of the hybrid that] is capable of being extended via a polymerase to form a complement of the second portion of the first oligonucleotide;

(iii) extending via a polymerase the 3' terminus of the second portion of second oligonucleotide and forming a complement of the second portion of the first oligonucleotide, thus producing an amplicon;

(v) amplifying the amplicon and producing an amplification product; and

(vi) detecting the amplification product, wherein the detection of the amplification product indicates the presence of the analyte in the sample.

78. (Currently Amended) A method of detecting an analyte in a sample, comprising:

(i) combining:

(a) an analyte;

(b) a first proximity member, comprising a first analyte-specific binding entity and a [first] single stranded first oligonucleotide comprising, from 5' to 3', a first portion and a second portion wherein the first analyte-specific binding entity is capable of forming a complex with the analyte and is conjugated to the first oligonucleotide;

(c) a second proximity member, comprising a second analyte-specific binding entity and a [second] single stranded second oligonucleotide comprising, from 5' to 3', a first portion and a second portion, wherein the second analyte-specific binding entity is capable of forming a complex with the analyte and is conjugated to the second oligonucleotide, wherein the second portion of the first oligonucleotide is capable of hybridizing to the second portion of the second oligonucleotide and the first analyte-specific binding entity and/or second analyte-specific binding entity is/are a protein[:] or proteins which is/are capable of directly binding to the analyte;

(ii) forming a complex comprising the analyte, the first proximity member, and the second proximity member, wherein the complex contains a hybrid comprising the second portion of the first oligonucleotide and the second portion of the second oligonucleotide[,wherein upon hybridization the 3' terminus of the second portion of the second oligonucleotide is capable of being extended via a polymerase to form a complement of the second portion of the first oligonucleotide];

(iii) producing an amplicon comprising: (i) adding a third oligonucleotide and forming a hybrid between the first portion of the first oligonucleotide and the third oligonucleotide and (ii) ligating the 3' terminus of the second oligonucleotide to the 5' terminus of the third oligonucleotide;

(iv) amplifying the amplicon and producing an amplification product; and

(vi) detecting the amplification product, wherein the detection of the amplification product indicates [detection] the presence of the analyte in the sample.

3. The following is an examiner's statement of reasons for allowance:

Claims 1-14, 16-21, 24-27, 29, 30, 74, and 78 are allowable in light of applicant's amendment filed on November 23, 2010 and the examiner's amendment. The rejections under 35 U.S.C 112, second paragraph have been withdrawn in view of the applicant's amendment and the examiner's amendment. Based on steps (i) and (ii) of claims 74 and 78, the first and/or second analyte-specific binding entity, which is/are a protein or proteins, must directly bind to the analyte in a complex comprising the analyte, the first proximity member, and the second proximity member. The closest prior art in the record is Kurn (US Patent No. 6,815,164, filed on October 9, 2001). This prior art does not teach or suggest step (iii) of claim 1 and combination of steps (i) and (ii) of claims 74 and 78. This prior art either alone or in combination with the other art in the record does/do not teach or reasonably suggest a method of detecting an analyte in a sample which comprises all limitations recited in claims 1, 74, and 78.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance".

4. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30

(November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is (571)273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (571)272-0746. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen, can be reached on (571)272-0731.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Frank W Lu /
Primary Examiner, Art Unit 1634
December 3, 2010